

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
22 April 2004 (22.04.2004)

PCT

(10) International Publication Number  
**WO 2004/032882 A2**

(51) International Patent Classification<sup>7</sup>: **A61K**

(21) International Application Number:  
PCT/US2003/033317

(22) International Filing Date: 10 October 2003 (10.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/417,548 10 October 2002 (10.10.2002) US

(71) Applicant (for all designated States except US):  
**SMITHKLINE BEECHAM CORPORATION**  
[US/US]; One Franklin Plaza, Philadelphia, PA 19101  
(US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BROWN, Matthew**,  
Lee [US/US]; c/o GlaxoSmithKline, Five Moore Drive,  
PO Box 13398, Research Triangle Park, NC 27709 (US).  
**CHEUNG, Mui** [CN/US]; c/o GlaxoSmithKline, Five  
Moore Drive, PO Box 13398, Research Triangle Park, NC  
27709 (US). **DICKERSON, Scott, Howard** [US/US];  
c/o GlaxoSmithKline, Five Moore Drive, PO Box 13398,  
Research Triangle Park, NC 27709 (US). **GAUTHIER**,  
**Cassandra** [US/US]; c/o GlaxoSmithKline, Five Moore  
Drive, PO Box 13398, Research Triangle Park, NC 27707  
(US). **HARRIS, Philip, Anthony** [GB/US]; c/o Glaxo-  
SmithKline, Five Moore Drive, PO Box 13398, Research  
Triangle Park, NC 27709 (US). **HUNTER, Robert, Neil**,  
**III** [US/US]; c/o GlaxoSmithKline, Five Moore Drive,  
PO Box 13398, Research Triangle Park, NC 27709 (US).  
**PACOFISKY, Gregory** [US/US]; 510 Polk Street, Raleigh,

NC 27604 (US). **PEEL, Michael, Robert** [GB/US]; c/o  
GlaxoSmithKline, Five Moore Drive, PO Box 13398,  
Research Triangle Park, NC 27709 (US). **STAFFORD**,  
**Jeffrey, Alan** [US/US]; c/o GlaxoSmithKline, Five Moore  
Drive, PO Box 13398, Research Triangle Park, NC 27709  
(US).

(74) Agents: **LEVY, David, J. et al.**; c/o GlaxoSmithKline,  
Corporate Intellectual Property Department, Five Moore  
Drive, PO Box 13398, Research Triangle Park, NC 27709  
(US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,  
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,  
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,  
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,  
RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,  
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,  
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished  
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: **CHEMICAL COMPOUNDS**

(57) Abstract: Oxazole derivatives, which are useful as VEGFR2, CDK2, and CDK4 inhibitors are described herein. The described invention also includes methods of making such oxazole derivatives as well as methods of using the same in the treatment of hyper-proliferative diseases.



**WO 2004/032882 A2**

# INTERNATIONAL SEARCH REPORT

International application No.

/ 503/33317

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : C07D 263/30; A61K 31/421 US CL : 548/233, 234; 514/377 According to International Patent Classification (IPC) or to both national classification and IPC														
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 548/233, 234; 514/377 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EAST, CAS ONLINE														
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>A</td> <td>US 6,399,773 B1 (LIU et al) 04 June 2002 (04.06.2002), entire document.</td> <td>1-44</td> </tr> <tr> <td>A</td> <td>US 6,197,975 B1 (GOULET et al) 06 March 2001 (06.03.2001), entire document.</td> <td>1-44</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	A	US 6,399,773 B1 (LIU et al) 04 June 2002 (04.06.2002), entire document.	1-44	A	US 6,197,975 B1 (GOULET et al) 06 March 2001 (06.03.2001), entire document.	1-44			
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.												
A	US 6,399,773 B1 (LIU et al) 04 June 2002 (04.06.2002), entire document.	1-44												
A	US 6,197,975 B1 (GOULET et al) 06 March 2001 (06.03.2001), entire document.	1-44												
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.														
<table border="0"> <tr> <td colspan="2">           * Special categories of cited documents:         </td> <td>           "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention         </td> </tr> <tr> <td>           "A" document defining the general state of the art which is not considered to be of particular relevance         </td> <td>           "E" earlier application or patent published on or after the international filing date         </td> <td>           "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone         </td> </tr> <tr> <td>           "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)         </td> <td>           "O" document referring to an oral disclosure, use, exhibition or other means         </td> <td>           "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art         </td> </tr> <tr> <td>           "P" document published prior to the international filing date but later than the priority date claimed         </td> <td>           "&amp;" document member of the same patent family         </td> <td></td> </tr> </table>			* Special categories of cited documents:		"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"A" document defining the general state of the art which is not considered to be of particular relevance	"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"O" document referring to an oral disclosure, use, exhibition or other means	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family	
* Special categories of cited documents:		"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention												
"A" document defining the general state of the art which is not considered to be of particular relevance	"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone												
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"O" document referring to an oral disclosure, use, exhibition or other means	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art												
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family													
Date of the actual completion of the international search 12 April 2004 (12.04.2004)		Date of mailing of the international search report 27 MAY 2004												
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Golam M M Shameem Telephone No. (571) 272-1600												

Form PCT/ISA/210 (second sheet) (July 1998)

BEST AVAILABLE COPY